R_1 and R_2 are each independently a monodentate ligand or together form a bidentate ligand;

R_3 and R_4 are each independently a monodentate ligand or together form a bidentate ligand; and

R_5 is a monodentate ligand, or is absent.

Remarks

Claims 1-5, 9, 10, and 15 remain pending in the application after entry of this amendment. Claims 6-8, 11-14, and 16-24 have been cancelled herein. Claim 1 has been amended as shown above. The claims were amended to more fully clarify the invention. No new matter has been added by the amendments made above. Favorable reconsideration is respectfully requested in light of the above amendments and the following comments.

Claim 1 is rejected under 35 U.S.C. § 112, second paragraph. Applicants respectfully traverse this rejection.

Claims 1-5, 9, 10, and 15 are rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over WO 00/35930. Applicants respectfully traverse this rejection.

35 U.S.C. § 112 Rejection

Claim 1 is rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner asserts that claim 1 is confusing, and apparently should contain "amount" after "inhibiting". Applicants have amended claim 1 in accordance with the Examiner's suggestion, and respectfully requests the withdrawal of this rejection.

35 U.S.C. § 102 or 103 Rejection

Claims 1-5, 9, 10, and 15 are rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over WO 00/35930. The Examiner asserts that WO 00/35930 explicitly discloses cancer treating efficacy of VDacac (also designated as $VCp_2(acac)$). The Examiner then argues that although the cited reference does not explicitly state that the cancer treating efficacy is obtained though inhibition of angiogenesis, killing or inhibiting cancer cells would necessarily encompass inhibition of mitosis or meiosis, and therefore the claims are anticipated or at the very least rendered obvious.

Applicants claim a method of inhibiting angiogenesis in a cell. Angiogenesis is the process of new vessel formation (page 1, line 10). WO 00/35930 discloses treating cancer cells only, and does not disclose inhibition of angiogenesis in cancer cells or otherwise. The Examiner asserts that killing or inhibiting cancer cells would necessarily encompass inhibition of angiogenesis of the cancer cells. Applicants respectfully disagree with this position, because although a dead cancer cell cannot undergo angiogenesis, the death of the cancer cell may have nothing to do with the cancer cell not undergoing angiogenesis, and the death of a cancer cell has no bearing on an activity that all cells go through. Because WO 00/35930 does not disclose anything regarding angiogenesis, and is only concerned with cancer cells, Applicants respectfully assert that WO 00/35930 does not anticipate the present claims.

WO 00/35930 also does not render the pending claims obvious. In order to establish *prima facie* obviousness, three basic criteria must be met, namely: (1) there must be some suggestion or motivation to combine the references or modify the reference teaching; (2) there must be a reasonable expectation of success; and (3) the reference or references when combined must teach or suggest each claim limitation. Applicants submit that the Office Action failed to state a *prima facie* case of obviousness, and therefore the burden has not properly shifted to Applicants to present evidence of nonobviousness.

One of the goals of WO 00/35930 is to develop anti-cancer therapies that have "efficient cytotoxicity against tumor cells" (page 1, lines 11-15). Although WO 00/35930 discloses treating cancer cells with VDacac, it is silent regarding the specific biological

mechanism that is affected. Based on the goal that is discussed above, one could assume that the cancer cell is being killed, that the VDacac is acting as a cytotoxic agent. There are numerous ways that a cell can be killed including for example: the cell membrane can be ruptured, or otherwise impaired, one of the multitude of necessary activities of the cell can be shut down or otherwise impaired, or the cell can be deprived of a necessary item. WO 00/35930 is silent regarding the specific cytotoxic pathway that VDacac undertakes in a cancer cell.

As discussed above, one goal of the agent in WO 00/35930 was for it to have a cytotoxic effect. The goal of inhibiting angiogenesis may not be to kill the cells, but only to halt their progression. If the progression and infiltration of cancer cells is inhibited, other treatments may be much more effective. Examples of such other treatments include but are not limited to removal of the tumor through surgical methods, targeted drug delivery, or radiation treatment. Therefore, the goal of inhibiting angiogenesis may not be to kill the cell. Therefore, one of skill in the art, given the disclosure of WO 00/35930, would not necessarily have considered the inhibition of angiogenesis as a method to be used to kill cancer cells.

Furthermore, WO 00/35930 is concerned strictly with cancer cells. One of skill in the art would not look to teachings regarding agents with cytotoxic effects against cancer cells to suggest methods of affecting a specific activity of that cell that was not discussed at all in the disclosure.

The present claims are directed to inhibiting angiogenesis. Angiogenesis is a necessary process if a tumor is growing and expanding its size. If angiogenesis is not taking place, a tumor can only expand to a certain size that is dictated, at least in part, by the vascularization of the tumor. A tumor that is not undergoing angiogenesis is not necessarily going to die, it will only cease to expand and infiltrate further tissue. WO 00/35930 does not disclose anything regarding maintaining a tumor at its current size. Therefore, WO 00/35930 fails to disclose or suggest all of the elements of the pending claims, and does not render them obvious.

Based on the above remarks, Applicants respectfully request the withdrawal of the obviousness rejection of claims 1-5, 9-10, and 15.

Conclusion

In view of the amendments and comments presented herein, favorable reconsideration in the form of a Notice of Allowance is respectfully requested.

Respectfully submitted,

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Date: October 2, 2002

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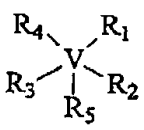
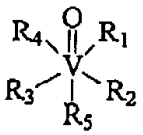
Marked up version of claim:

Please cancel claims 6-8, 11-14, and 16-24 without prejudice or disclaimer of the subject matter contained therein. Please amend claim 1 as given below.

1. (Amended) A method for inhibiting angiogenesis comprising administering to a subject an effective angiogenesis inhibiting amount of a vanadium compound having the following structure:



(I)



(II)

wherein,

R_1 and R_2 are each independently a monodentate ligand or together form a bidentate ligand;

R_3 and R_4 are each independently a monodentate ligand or together form a bidentate ligand; and

R_5 is a monodentate ligand, or is absent.